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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,764	09/27/2000	Joseph R. Pisegna	M-8978 US	7433

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/18/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/671,764	PISEGNA ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,20-29 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,20-29 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 1-12, 20-29 and 31 are pending.

Applicants' amendment filed on June 2, 2003 (Paper No. 18) is acknowledged, and applicants' response has been fully considered. Claims 1, 2, 20, 21 and 31 have been amended, and claims 13-19 and 30 have been cancelled. Therefore, claims 1-12, 20-29 and 31 are examined.

Oath/Declaration

2. Applicants indicate a new oath is being executed and will be forwarded when it becomes available.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

3. The previous rejection of claims 1-12, 21-29 and 31, under 35 U.S.C. § 112, second paragraph, is withdrawn in view of applicants' amendment to the claim and applicants' response at pages 5-6 in Paper No. 18.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-12, 20-29 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the efficacy of a specific gastric H+/K+-ATP pump inhibitor (PPI) such as pantoprazole in mammal having a pathology of excess

gastric acid secretion by administering pentagastrin in conjunction with pantoprazole, or a kit for the treatment of pathology of excess gastric acid secretion, comprising a container containing a specific PPI such as pantoprazole or omeprazole and a container containing pentagastrin; or, a method of increasing the efficacy of a PPI, BY1023/SK&F 96022 (pantoprazole) in mammal having a pathology of excess gastric acid secretion by administering pentagastrin in conjunction with pantoprazole, or of increasing the efficacy of omeprazole in animal model by administering specific gastrin analogs in conjunction with omeprazole as indicated in the prior art, does not reasonably provide enablement for a method of increasing the efficacy of a PPI in mammal by administering gastrin or an analog of gastrin or pentagastrin in conjunction with the PPI, or a kit for the treatment of pathology of excess gastric acid secretion, comprising a PPI and gastrin or an analog of gastrin or pentagastrin, where the PPI or the analog of gastrin or pentagastrin is not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-12, 20-29 and 31 encompass a method of increasing the efficacy of a PPI in mammal by administering an analog of gastrin or pentagastrin in conjunction with the PPI (claims 1-12), or a kit for the treatment of pathology of excess gastric acid secretion, comprising a container containing a PPI and a container containing gastrin, or an analog of gastrin or pentagastrin (claims 20-29 and 31). The specification, however, only discloses cursory conclusions without data supporting the findings, which state that the present invention provides a method of treating pathological conditions characterized by excess gastric acid secretion, in particular the method of administering a gastrin, a pentagastrin or an analog thereof in

conjunction of a PPI, which will result in increased efficacy, or a kit for the treatment of pathology characterized by excess gastric acid secretion, comprising a container containing a PPI and a container containing pentagastrin (page 2, line 7-page 4, line 2). There are no indicia that the present application enables the full scope in view of a method of increasing the efficacy of a PPI in mammal and a kit for the treatment of pathology of excess gastric acid secretion as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding analogs of gastrin or pentagastrin and PPIs, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for administering pantoprazole to humans having pentagastrin-induced gastric acid secretion (Example 1).

(3). The state of the prior art and relative skill of those in the art:

The prior art (e.g., Simon *et al.* , Aliment. Pharmacol. Therap. 4, 239-245 (1990)) indicates the effect of a PPI, BY1023/SK&F 96022 on the pentagastrin-stimulated acid secretion in healthy male volunteers; Murphy *et al.* (U. S. Patent 4,997,950) teach the use of analogs from C-terminus of gastrin in adjunctive therapy with a PPI, omerprazole in animal models. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide teachings on the use of various analogs of gastrin or pentagastrin in conjunction with various PPIs, and the effects of the analog to increase the efficacy of the PPI in mammals to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method of increasing the efficacy of a PPI in mammal by administering an analog of gastrin or pentagastrin in conjunction with the PPI, or a kit for the treatment of pathology of excess gastric acid secretion, comprising a PPI and an analog of gastrin or pentagastrin, however, the treating conditions for various analogs of gastrin or pentagastrin to increase the efficacy of a PPI and the in vivo effects of these analogs are not adequately described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of increasing the efficacy of a PPI in mammal by administering gastrin, or an analog of gastrin or pentagastrin in conjunction with the PPI, or a kit for the treatment of pathology of excess gastric acid secretion, comprising a PPI and gastrin, or an analog of gastrin or pentagastrin. The specification indicates the pentagastrin can be

administered before, simultaneously with or after the PPI administration, and the general dosages for pentagastrin, gastrin, or analogs thereof (page 2), Example 1 demonstrates single doses of *i.v.* pantoprazole ranging 20-120 mg suppressed gastric acid secretion in a dose-dependent manner in healthy subjects subject to continuous pentagastrin-induced hypersecretion. However, the specification has not demonstrated using any analog of gastrin or pentagastrin in a specific dose range to increase the efficacy of a PPI except for the use of pentagastrin and pantoprazole. Moreover, there are no working examples indicating the effects of analogs of gastrin or pentagastrin in increasing the efficacy of various PPIs in mammals. Since the specification fails to provide sufficient teachings on the treating conditions for various analogs of gastrin or pentagastrin in conjunction with different PPI, and the in vivo effects of these analogs of gastrin or pentagastrin, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various analogs of gastrin or pentagastrin in the claimed method.

(6). Nature of the Invention

The scope of the claims encompasses a method of increasing the efficacy of a PPI in mammal by administering an analog of gastrin or pentagastrin in conjunction with the PPI, but the specification does not demonstrate using various analogs of gastrin or pentagastrin in conjunction with various PPIs in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broader than the enabling disclosure. The working examples do not demonstrate the claimed methods, the outcome of the treatment is unpredictable, and the teaching in the specification is limited, therefore, it is necessary to have

additional guidance and to carry out further experimentation to assess the effects of using various analogs of gastrin or pentagastrin in the method of increasing efficacy of various PPIs.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-12 are indefinite because the claims lack essential steps in the method of increasing the efficacy of a gastric H^+/K^+-ATPase pump inhibitor in mammal. The omitted step is effective amounts of a gastric proton pump inhibitor and a pentagastrin, a gastrin or a gastrin analog used in the claimed method. Claims 2-12 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2, 5, 6, 7 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Simon *et al.* (Aliment. Pharmacol. Therap. 4, 239-245 (1990)).

Simon *et al.* teach the effects of the H^+/K^+-ATPase inhibitor, BY1023/SK&F 96022 on the pentagastrin-stimulated acid secretion in healthy male volunteers, and intravenous administration of BY1023/SK&F 96022 induced a rapid and dose-dependent inhibition of pentagastrin-stimulated acid secretion, where the inhibitory effect lasted longer than the measurement period, 3 hours (abstract, page 241, Fig. 2; claims 1, 2, 5 and 11). Pentagastrin is continuously infused, and one hour after the start of the pentagastrin infusion, the proper dose of BY1023/SK&F 96022 or placebo is administered intravenously (page 241, claims 6 and 7).

In response, applicants indicate the claim has been amended to recite "the efficiency of said gastric proton pump inhibitor is increased"; Simon *et al.* simply investigate the efficacy of the PPI, BY1023/SK&F 96022, the PPI was administered to human volunteers that acid secretion had been induced using pentagastrin, and Simon *et al.* does not show the effect of BY1023/SK&F 96022 in subjects that were not administered pentagastrin; and Simon *et al.* teach the use of pentagastrin to induce the pathological state which is then mitigated by the administered PPI, while the presently claimed method cites the administration of gastrin, pentagastrin or gastrin analog with a PPI to increase the efficacy of the PPI, i.e., to reduce or inhibit the pathological condition (pages 7-8 of the response). The response has been fully considered, however, the argument is not persuasive because Simon *et al.* teach administering pentagastrin prior to and simultaneously to the administration of the PPI to a pathological state of human volunteers, which has the same steps used in the claimed method, thus the efficiency of the PPI would be expected to increase. Moreover, the reference also shows the inhibitory effect lasted longer than the measurement period (page 242, first paragraph; Fig 2), which indicates the prolonged effect.

7. Claims 1 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Murphy *et al.* (U. S. Patent 4,997,950).

Murphy *et al.* teach analogs from C-terminus of gastrin act as potent and specific antagonists of gastrin-stimulated acid secretion (column 1, lines 6-10), these analogs can be used in adjunctive therapy with drugs such as omeprazole, a H^+/K^+-ATPase inhibitor in animal models (column 2, lines 24-31; column 5, claims 1 and 12). The administration of gastrin analogs in conjunction with omeprazole to animals would be expected to have synergistic effect because Murphy *et al.* teach administering the same compounds as the claimed method, the gastrin analog would be expected to have the same effect toward the PPI, thus, the claimed invention is anticipated by the reference.

In response, applicants indicate Murphy *et al.* fail to teach the disclosed peptides, when administered in conjunction with a PPI increase the efficacy of that PPI, the PPI and the gastrin analogs disclosed by Murphy *et al.* could function by different mechanisms and have no effect on each other (pages 8-9 of the response). The response has been fully considered, however, the argument is not persuasive because the reference teach administering the same compounds to animals as the claimed method, the administration of gastrin analogs would be expected to increase the efficacy of omeprazole.

Conclusion

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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August 14, 2003

Christopher S. F. Low

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